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The prevalence of hypertension among patients with Type 1 diabetes and its associated factors in Saudi Arabia

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ABSTRACT

Objective: The present study was conducted to determine the prevalence of hypertension among patients with T1DM and its associated factors in Saudi Arabia. *Methodology*: An analytic cross-sectional study was conducted among patients with T1DM at a tertiary hospital in Riyadh, Saudi Arabia. The data were collected via a telephone survey and electronic medical record. Adult patients (>18 years) with T1DM who followed up at the tertiary hospital were enrolled in this research. Data regarding patient variables were collected (e.g.,diagnosis of hypertension, duration of diabetes, smoking, glycosylated hemoglobin (HbA1c), age, sex, body mass index (BMI), urine albumin to creatinine ratio (UACR), and hemoglobin). *Results:* A Total of 240 patients (55.4% females, 44.6% males) with T1DM were included in the study. Mean age, HbA1C, and BMI were 30.6±9.6 years, 8.8±1.98 %, and 26.2±6.1 kg/m^2, respectively. The prevalence of hypertension in the study was 17.9%. The study revealed that age (p = 0.000), BMI (p = 0.000), duration of diabetes (p = 0.000), eGFR (p = 0.000), triglycerides (p = 0.000), and retinopathy (p = 0.000) have significant association with hypertension among the patients with T1DM. However, Gender (p = 0.462), HbA1c (p = 0.243), LDL (p = 0.454), HDL (p = 0.086), and smoking (p = 0.986) showed no significant association with hypertension among T1DM patients. *Conclusion:* Hypertension is prevalent among patients with T1DM in Saudi Arabia, warranting making certain policies to hamper the coexistence of these two risk factors of increased morbidity and mortality.

Keywords: Hypertension, Type I Diabetes Mellitus, Albuminuria, Glomular Filtration rate, Retinopathy

1. INTRODUCTION

Type 1 diabetes (T1DM) is one of the two major types of diabetes characterized by the absence of endogenous insulin and hyperglycemia, a

soaring epidemic in Saudi Arabia (Katsimardou et al., 2020; Robert et al., 2018). It is an endocrine, metabolic disorder that affects both children and adolescents (Robert et al., 2018). Approximately 451 million adults suffer from diabetes worldwide, where T1DM contributes 5–10% of all diabetes cases (Mobasseri et al., 2020; Lin et al., 2020). In the United States of America (USA), T1DM and type 2 diabetes (T2DM) contribute to 6% and 91% of all diabetes cases, respectively (Bullard et al., 2018). The incidence of T1DM is on the rise in the Kingdom of Saudi Arabia (KSA). In KSA, the incidence of T1DM has been reported to be up to 36.99 per 100,000 children (Robert et al., 2018). It has also been indicated that the incidence of T1DM in Saudi Arabia is higher than that reported in other countries of the world (Mobasseri et al., 2020).

Diabetes is a serious health concern as it increases mortality and reduces life expectancy (Lin et al., 2020). In 2019, diabetes resulted in 1.5 million deaths globally (World Health Organization, 2021). Genetic and environmental factors are usually involved in the development of T1DM (Simmons et al., 2015). Hypertension is a modifiable risk factor for cardiovascular disease (CVD) and all-cause morbidity and mortality (Oparil et al., 2018). Globally, 3.5 billion and 874 million individuals had non optimal systolic blood-pressure (> 110–115 mmHg) and hypertension (> 140 mmHg), respectively (Oparil et al., 2018). Non-optimal blood pressure significantly contributes to all-cause mortality, resulting in approximately 9.4 million deaths and the loss of 212 million healthy life years every year (Forouzanfar, 2016). Similarly, hypertension results in 7.8 million deaths in the world annually (Mills et al., 2020). Hypertension leads to a large burden of CVD and premature deaths, where "ischemic heart disease (IHD) and stroke" are the main contributors to hypertensive deaths (Gupta & Xavier, 2018).

Risk factors of hypertension include high sodium or low potassium taking, consuming alcohol, shortage of physical exercises, overweight, obesity, unhealthy diet, cigarette smoking, air pollution, stress, and sleep disorders (Mills et al., 2020). Hypertension and diabetes (T1DM and T2DM) are associated with premature CVD (Mills et al., 2020; Schofield & Soran, 2019). Thus, the coexistence of hypertension and T1DM is a major risk of CVD and mortality (Lee et al., 2015). The frequency of hypertension among diabetic patients is double when comparingwith non-diabetic patients (Petrie et al., 2018).

Hyperglycemia is a risk factor for incident hypertension among patients with T1DM (De Boer et al., 2008). In addition, hypertension contributes to micro- and macro-vascular complications of diabetes, resulting in increased cardiovascular morbidity and mortality (De Boer et al., 2008). Proper management of hyperglycemia in patients with T1DM may prevent vascular changes, leading to a reduced risk of developing hypertension. Cardiovascular disease is the major cause of morbidity and mortality among patients with diabetes and hypertension. Type 1 diabetes is one of the most common chronic diseases among children, affecting 6–16% of children (Downie et al., 2018). Hypertension, a reversible CVD risk agent, might be unnoticed and be left untreated among patients with T1DM. Poor glycaemic control, obesity, and genetic factors are major risk factors of hypertension among patients with T1DM (Downie et al., 2018). Sustained hyperglycemia results in impaired endothelial and vascular dysfunction, such as increased vascular thickness and impaired vasodilatation, leading to the development of hypertension (Downie et al., 2018).

Diabetes and hypertension are prevalent chronic diseases in KSA. Diabetes is growing at a worrying rate in Saudi Arabia (Robert et al., 2020). There is alack of data regarding how much prevalent is hypertension among patients with T1DM in Saudi Arabia. Therefore, this cross-sectional study was designed to determine the prevalence of hypertension in T1DM and its associated factors in Saudi Arabia.

2. METHODOLOGY

Study design and setting

This analytic cross-section was a study conducted among patients with T1DM at a tertiary hospital in Riyadh, Saudi Arabia. The data were collected via a telephone survey and electronic medical record. We included adult patients (>18 years) suffering from T1DM who followed up at the tertiary hospital. We excluded all patients who had less than two visits to the clinic or any patient with incomplete data in the electronic medical records.

The Institutional Review Board approved the study at the College of Medicine, King Saudi University (Project number E-20-5530). Detailed information regarding the purpose of the study was given to all participants, and verbal consent was obtained from all individuals before initiating the telephone survey.

Data collection and laboratory measurements

A list of 900 patients with T1DM was obtained from the electronic health system from "January 2018 to December 2020". Those patients not meeting the inclusion criteria were excluded, and the next patient on the list was chosen. The first 320 patients fulfilled the criteria and were eligible for telephonic interviews. Variables like a diagnosis of hypertension, duration of diabetes, and smoking were gathered by a structured interviewer-administered questionnaire among the selected 320 individuals. Eighty patients

refused to participate in the study or could not be reached by phone. The remaining 240 participants completed the telephone survey and were included for analysis. The rest of the data were extracted from the electronic clinical records, which includesHbA1c, age, sex, body mass index (BMI) (kg/m^2), urine albumin to creatinine ratio (UACR), and hemoglobin (g/L).

The last serum creatinine level measured for every individual was used to calculate the estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration formula based on serum creatinine (CKD-EPICr). Albuminuria was classified into normal (UACR <30 mg/g), microalbuminuria (UACR between 30 and 299mg/g), and macroalbuminuria (UACR ≥ 300 mg/g). The chronic kidney disease was defined as eGFR <60 ml/min/1.73m^2 and/or presence of albuminuria >30 mg/g on two occasions three months apart.

Sample size

A standard sample size equation "n = z2 p(1-p)/e2" was used to calculate the sample size. We used the 14.3% proportion of hypertension in diabetic patients, as previously reported (Norgoord et al., 1990). Using a 90% confidence interval and a 4% margin of error, the sample size was estimated to be 206.

Statistical Analysis

The study used the "Statistical Package of Social Sciences" (SPSS) (v.26.0, IBM Corporation, New York, USA) to analyze the gathered data of type 1 diabetic patients. The descriptive statistics were used to describe the patients' clinical and background data. In addition, independent samples t-test and Chi-square test of independence were used to compare the clinical and background characteristics of the enrolled T1DM patients. Both bar and stacked bar charts were used to plot the prevalence of hypertension based on patients' age groups and BMI categories and the albuminuria classes' prevalence among controlled and uncontrolled hypertension patients' categories.

3. RESULTS

The study population

A total of 240 patients with T1DM were included and analyzed in this study. The results presented in Table 1 represent the clinical and background characteristics of the study participants. About 55.4% (n=133) of the participating patients were females, whereas 44.6% (n=107) were males. Mean age, HbA1C and BMI were 30.6±9.6 years, 8.8±1.98%, and 26.2±6.1 kg/m^2, respectively. In addition, the mean duration of being diabetic was 13.5±8.04, and the mean value of eGFR CKD EPI was 113.8±22.6. Exploring the lipid profile data of the enrolled patients indicated that mean total cholesterol was 4.6±1.02, the mean triglycerides value was 1.08±0.59, mean Low-Density Lipoprotein (LDL) was 2.62±0.87, and the mean high-density lipoprotein (HDL) was 1.50±0.41. Exploring the prevalence of retinopathy revealed that 21.7% (n=52) had retinopathy, whereas 78.3% (n=188) had no retinopathy. About 20.8% (n=50), 76.7% (n=184), and 2.5% (n=6) were smokers, non-smokers, and ex-smokers, respectively.

Table 1 Clinical and background characteristics of the participants

Characteristics	N (%)	M ± SD
Sex		
Male	107 (44.6%)	
Female	133 (55.4%)	
Age		30.6±9.6
A1C mean		8.8±1.98
BMI mean		26.2±6.1
Diabetes duration		13.5±8.04
eGFR CKD EPI		113.8±22.6
A/C Ratio		100.6±322.5
Total cholesterol		4.6±1.02
TG		1.08±0.59
LDL		2.62±0.87
HDL		1.50±0.41
Retinopathy		
Yes	52 (21.7%)	

No	188 (78.3%)	
Smoking Yes No Ex-smoker	 50 (20.8%) 184 (%76.7) 6 (2.5%)	

The prevalence of hypertension

The prevalence of hypertension in the cohort was 17.9% (n=43). The results in Table 2 represent independent samples t-test and Chi-square test of independence to compare hypertensive and non-hypertensive patients. Moreover, the results showed that diabetes duration differed significantly between hypertensive patients (19.62±9.40) and non-hypertensive patients (12.17±7.06) (t=-5.881, p=0.000). Moreover, there was a significant statistical difference in triglycerides level between hypertensive (1.31±0.64) and non-hypertensive patients (1.04±0.58) (t=-2.714, p=0.007). However, there were no remarkable differences in HbA1c, total cholesterol, LDL, HDL, and hemoglobin between hypertensive and non-hypertensive patients.

Chi-square analysis showed a significant difference between hypertension and retinopathy as 41.9 % of patients with T1DM and hypertension developed retinopathy compared to 17.3% in type 1 diabetic patients without hypertension (χ^2=12.5867, p=0.000). Finally, there was a significant association between eGFR, albuminurea, age, and BMI with hypertension. However, there was no sign of gender and smoking on the incidence of hypertension among T1DM patients. Among 43 hypertensive patients, there were 34 (79.1%) patients with controlled blood pressure in contrast to nine (21.9%) with uncontrol blood pressure.

Table 2 Comparison between type 1 patients with hypertension and no hypertension

	Hypertension Total: 43	Non hypertension Total= 197	X^2	t	P value
Age	36.46±10.9	29.35±8.8		-5.284	0.000
Gender Male Female	 17 (39.5%) 26 (60.5%)	 90 (45.7%) 107 (54.3%)	0.5404		0.462
A1C mean	9.16±1.98	8.77±1.98		-1.170	0.2431
BMI mean	30.17±8.79	25.43±4.98		-4.285	0.000
Diabetes duration	19.62±9.40	12.17±7.06		-5.881	0.000
eGFR CKD EPI	100.42±33.42	116.70±18.39		4.435	0.000
Normoalbuminuric UACR<30 Microalbuminuria /Macroalbuminuria UACR ≥30	17 (39.5%) 26 (60.5)	139(70.6%) 58 (29.4%)	14.932		0.000
Total cholesterol	4.51±1.51	4.65±0.88		0.816	0.4156
TG	1.31±0.64	1.04±0.58		-2.714	0.007
LDL	2.53±1.30	2.64±0.75		0.749	0.4547
HDL	1.40±0.33	1.52±0.43		1.722	0.0864
Retinopathy Yes No	 18 (41.9%) 25 (58.1%)	 34 (17.3%) 163 (82.7%)	12.5867		0.000
Smoking Yes no	 9 (20.9%) 34 (79.1%)	 41 (20.8%) 156 (79.2%)	0.007		0.9862

Hypertension and chronic kidney disease

The eGFR is lower among hypertensive than in non-hypertensive patients (100.42 ± 33.42 vs. 116.70±18.39, t=4.435, p=0.000 (Table 2). The results shown in Figure (1) represent the prevalence of albuminuria classes based on hypertensive patients' gender. Around two-thirds of hypertensive patients presented with albuminuria (60%) compared with only (29%) of patients without hypertension (p = 0.000). Moreover, the prevalence of albuminuria was more in uncontrolled hypertensive (patients compared to patients with controlled hypertension (66.7% vs. 58.8%) (Figure 1).

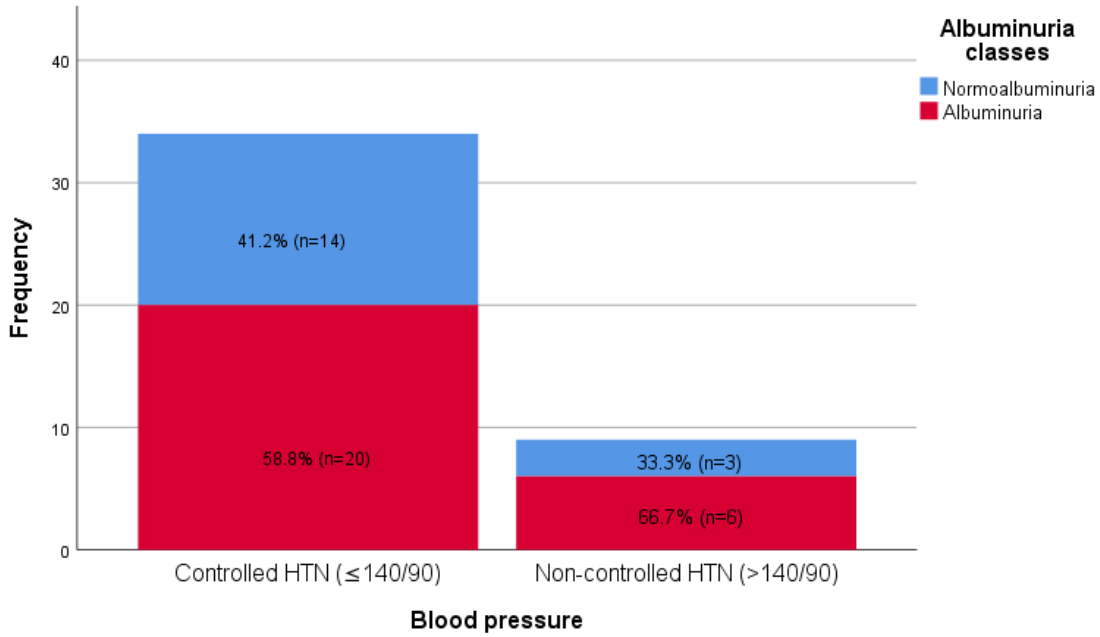

Figure 1 The proportion of controlled and uncontrolled hypertension with prevalence of albuminuria in each group

Hypertension and age

The results revealed that hypertension was higher in older diabetic patients (36.46±10.9) than non-hypertensive patients (29.35±8.8) (t=-5.284, p=0.000) (Table 2). A higher incidence was found among type 1 diabetic patients older than 44 years (34.8%), whereas the incidence rate of patients aged 18 to 25 years and 35 to 43 years was 23.3% for each group. The least incidence rate (18.6%) was among diabetic patients aged 26 to 34 years. More details about the prevalence of hypertension and age groups have been shown in Figure 2.

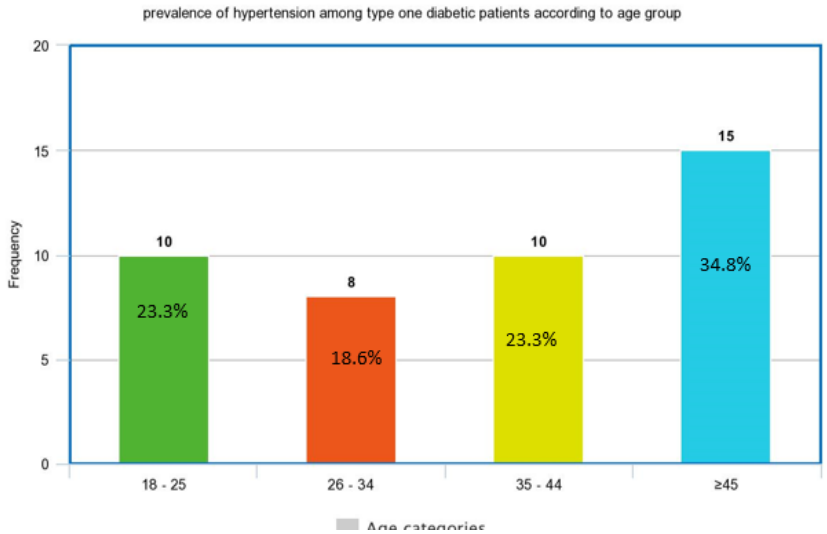

Figure 2 Prevalence of hypertension among type 1 DM patients according to age categories

Hypertension and BMI

Table 2 shows a significant difference in BMI between hypertensive patients and non-hypertensive patients (30.17 ± 8.79 vs. 25.43±4.98, t=-4.285, p=0.000). The results presented in Figure 2 show a stacked bar chart representing of hypertension prevalence based on type 1 diabetic patients' BMI categories. The prevalence of hypertension is directly correlated with the BMI category. The results showed that 11.1% of normal-weight patients were hypertensive, whereas 47%. 4 of morbidly obese patients have hypertension (Figure 3).

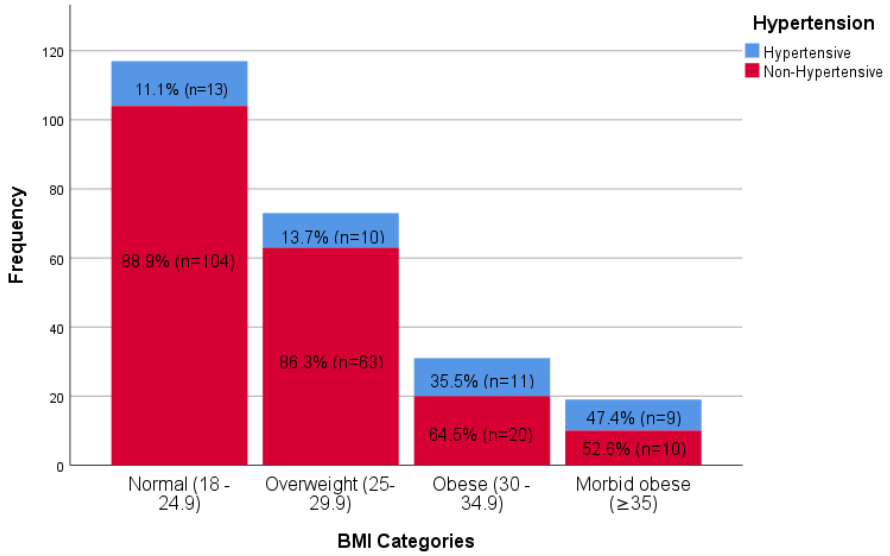

Figure 3 Prevalence of hypertension based on patients' BMI category

4. DISCUSSION

To our knowledge, this is the first study that determines the prevalence of hypertension among patients with T1DM and its associated factors in Saudi Arabia. The detected prevalence of hypertension among T1DM patients was 17.9%. In the study, age, BMI, duration of diabetes, decreased eGFR, albuminuria, TG, and retinopathy showed significant association with hypertension among the patients with T1DM. Other factors, such as gender, HbA1c, LDL, HDL, and smoking, showed no significant association with hypertension among T1DM patients.

In general, the prevalence of hypertension among diabetic patients is high compared to that in non-diabetic patients. It is important to know as hypertension accelerates the "microvascular and macrovascular complications" of diabetes, such as diabetic neuropathy, nephropathy, and retinopathy (Norgoord et al., 1990). Norgaard et al., (1990) studied 10,202 persons from the general Danish population (aged 16–59 years) to find out the prevalence of hypertension among T1DM patients. They reported the prevalence of hypertension as 4.4% and 14.7% among the general population and T1DM patients, respectively. This finding is consistent with our results. Chillaron et al., (2011) conducted a cross-sectional study including 291 patients with T1DM to determine the prevalence of hypertension, its associated factors, and insulin resistance among type 1 diabetic patients in Spain. They reported hypertension among one-third of T1DM patients with a prevalence of 29.9% and a higher number of patients with diabetic complications, e.g., neuropathy, nephropathy, and retinopathy. In addition, they also reported insulin resistance in 61.4% and 40% of hypertensive and non-hypertensive patients, respectively. Maahs et al., (2005) carried out a case-control study in Colorado having 1416 individuals to compare prevalence, awareness, treatment, and hypertension control between T1DM patients and those without diabetes. They reported 43% and 15% hypertension prevalence among type 1 diabetic patients and non-diabetic individuals, respectively. There are several possible explanations for their study's higher prevalence of hypertension in type 1 DM patients than in our study. These factors include the patient's age and the duration of diabetes. In their study, the mean age was 37 years, and the duration was 23 years, but in our study, the mean age was 30 years, and the duration was 13 years.

Moreover, differences in how hypertension is defined might explain these disparities in prevalence between all previous studies. Some studies define hypertension after measuring the participants' blood pressure, which might be affected by the protocol and device they used in their study. For example, one study defined hypertension based on measuring blood pressure twice on one occasion only. Furthermore, a self-reported questionnaire, such as the one used in this study, might be used to define hypertension. Prevalence and severity of hypertension increase with advancing age among men and women (Lionakis et al., 2012). However, T1DM is a juvenile chronic metabolic disorder; however, as time passes, hypertension and its complications increase due to vascular impairment. Therefore, proper management of hyperglycemia may help prevent vascular damage and subsequent development of hypertension. Chillaron et al., (2011) also reported older age, male gender, higher BMI, and longer diabetes duration as significant associated factors of hypertension. However, the present study does not reveal significant differences regarding hypertension in type 1 diabetic patients between men and women. Hypertension, hyperglycemia, and macroalbuminuria strongly affect aortic stiffness, leading to CVD (Schnell et al., 2013).

Hypertension is a significant contributing factor to and consequence of chronic renal disease. A vicious cycle starts when decreasing kidney function results in increased blood pressure, resulting in further kidney injury and subsequent loss of function. If no nephropathy develops in patients with type 1 diabetics, these individuals often maintain a normotensive state (Oakley et al., 1974). Large trials were conducted to determine the benefit of lowering blood pressure on decreasing the adverse kidney outcome in type II diabetics. However, limited trials have been done to assess the efficacy of alternative blood pressure goals in reducing the risk of adverse kidney events in type 1 diabetic patients (Ku et al., 2016). The albuminuria and low eGFR are significantly more prevalent among the hypertensive group in this study. This result is in line with another study which showed that blood pressure and the likelihood of adverse renal outcomes are linearly related (Ku et al., 2016). Decreased eGFR is a risk factor for CVD morbidity and mortality, as well as progression to end-stage kidney disease (van der Meer et al., 2010).

Diabetes and hypertension are well-known risk factors for chronic kidney disease (CKD). It had been revealed that 30% and 40% of individuals with T1DM and T2DM develop microvascular changes, respectively (Nasri & Rafieian-Kopaei, 2015). Moreover, T1DM poses more risk for CKD than of T2DM (Van Buren & Toto, 2011). In the USA, diabetes and hypertension contribute to >50% of "end-stage renal disease (ESRD)" (Nasri & Rafieian-Kopaei, 2015). Early reduction in eGFR among T1DM patients is positively associated with ESRD (Radcliffe et al., 2017). Therefore, early detection with glycemic and blood pressure control among hypertensive patients with T1DM may help prevent or slow ESRD progression.

In almost 70 countries, the prevalence of obesity has increased twofold over the last two decades while rising in most other nations (GBD 2015, Obesity Collaborators, 2015). Furthermore, one study showed that BMI levels for patients with T1DM were remarkably raised compared to those for the general population (Fellinger et al., 2019). Unsurprisingly, the frequency of metabolic syndrome and hypertension is growing in type 1 diabetes in this setting. Our data showed a significant association between BMI and hypertension. This finding is in agreement with a previous study (Chillaron et al., 2011). Moreover, our result showed a direct correlation between BMI and the prevalence of hypertension. This emphasizes the need of weight management for patients with type 1 diabetes.

The present study revealed no significant association between gender, HbA1c, LDL, HDL, smoking, and albuminuria and hypertension among T1DM patients. However, Chillaron et al., (2011) have reported a significant association of male gender with hypertension among T1DM patients. Manicardi et al., (2016) evaluated gender differences among T1DM patients and reported a 29% lower risk of hypertension among women. One possible explanation for the non-significant result of gender in our study is that it could be affected by the prevalence of smoking which is similar in both groups. Molla et al., (2020) studied the effect of smoking on the complications of diabetes (either T1DM or T2DM). They reported that smoking was significantly associated with a history of hypertension among diabetic patients of both T1DM and T2DM.

The importance of the study is that it is a unique study that evaluated the prevalence of hypertension among T1DM patients and its related risk factors among the Saudi population. As the coexistence of diabetes and hypertension is a heavy burden on the healthcare system worldwide, the early detection, management, and stringent preventive measures against hypertension may reduce CVD morbidity and mortality.

This study's limitations are primarily due to the cross-sectional design of the present research. The findings presented here are only correlations from which no inferences about causality can be drawn. Moreover, another limitation of this study is that it is a single-center study, raising concerns regarding the generalizability of our findings. Therefore, studies are warranted at a large scale at multiple centers to determine the exact prevalence of hypertension and its associated factors among Saudi T1DM patients.

5. CONCLUSION

The prevalence of hypertension among T1DM patients is high among the Saudi population. Hypertension is an additional risk for CVD among T1DM patients. Therefore, early detection and management of hyperglycemia and proper treatment of hypertension and its related risk factors may reduce CVD risk and subsequent morbidity and mortality in Saudi Arabia.

Ethical Approval

This study was approved by the Institutional Review Board at the College of Medicine, King Saudi University (Project number E-20-5530).

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Authors' Contribution

The authors would like to declare that all authors had contributed equally in the production of this original manuscript through the process of formulating the research problem, developing the methodology, conducting the data collection and analysis, and interpreting findings.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Data and materials availability

All data associated with this study are present in the paper.

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